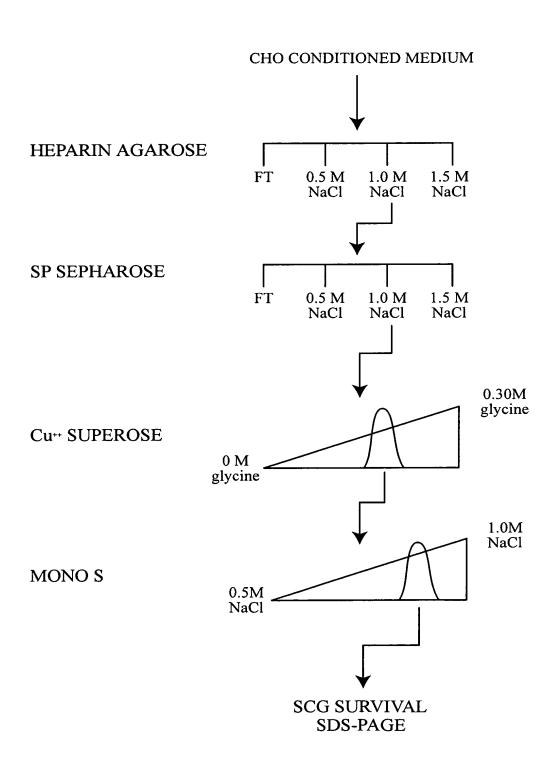


Title: Neurturin and Related Growth Factors

Inventor(s): Johnson et al.

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Figure 1

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fraction: ML 21 22 23 24 25 26 27 28 29 30 31 32



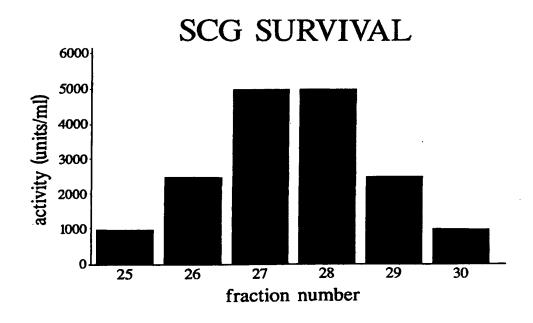


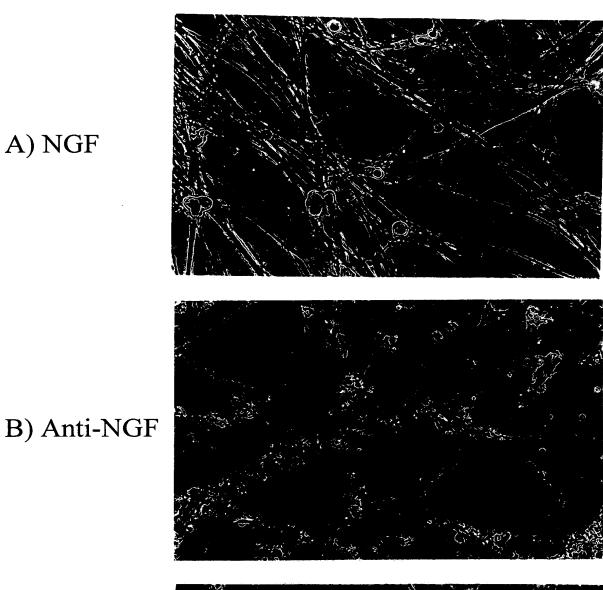
Figure 2

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C) Anti-NGF + Neurturin

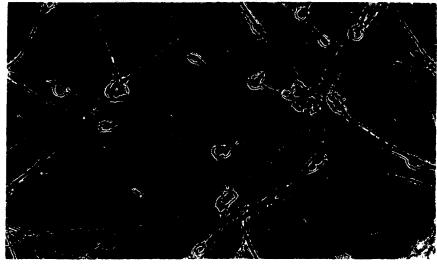


Figure 3

Neurturin and Related Growth Factors Title: Johnson et al. Inventor(s):

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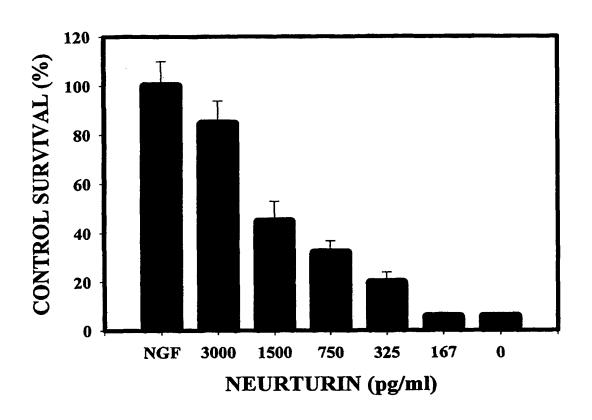


Figure 4

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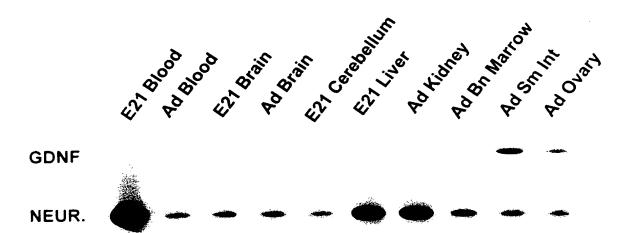
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                                                                                                                                        mGDNF
         S P D K Q A A A L P R R E R N R Q A A A A S P E N S R G K G
                                                                                                                                         rGDNF
1
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1
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1
         R R G Q R G K N R G C V L T A I H L N V T D L G L G Y E T K R R G Q R G K N R G C V L T A I H L N V T D L G L G Y E T K R R G Q R G K N R G C V L T A I H L N V T D L G L G Y E T K - - - A R L G A R P C G L R E L E V R V S E L G L G Y A S D - - - - P G A R P C G L R E L E V R V S E L G L G Y T S D
31
                                                                                                                                        anGDNF
31
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31
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1
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1
         E E L I F R Y C S G S C D A A E T T Y D K I L K N L S R N R E E L I F R Y C S G S C E S A E T M Y D K I L K N L S R S R E E L I F R Y C S G S C E A A E T M Y D K I L K N L S R S R E T V L F R Y C A G A C E A A A R V Y D L G L R R L R Q R R E T V L F R Y C A G A C E A A I R I Y D L G L R R L R Q R R
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                                                                                                                  DD N L V HGDNF
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                                                                                                                                        mGDNF
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                                                                                                                                         rGDNF
58
56
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Y H I L R K H S A K R C G C I
Y H I L R K H S A K R C G C I
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Neurturin and Related Growth Factors Title: Johnson et al.

Inventor(s):

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ATGAGGCGCTGGAAGGCAGCGGCCCTGGTGTCGCTCATCTGCAGCTCCCTGCTATCTGTC 60 Met Ang Ang Trp Lys Ala Ala Ala Leu Val Ser Leu Ile Cys Ser Ser Leu Leu Ser Val TGGATGTGCCAGGAGGGTCTGCTCTTGGGCCACCGCCTGGGACCCGCGCTTGCCCCGCTA 120 <u>Trp Met Cys Gln Glu Gly Leu Leu Leu Gly His Arq Leu Gly Pro Ala Leu Ala Pro Leu</u> CGACGCCCTCCACGCACCCTGGACGCCCGCATCGCCCCCCCGGCCCAGTĂTCGCGCTCTG 120 Ang Ang Pro Pro Ang Thr Leu Asp Ala Ang Ile Ala Ang Leu Ala Gln Tyr Ang Ala Leu CTCCAGGGCGCCCCGACGCGGTGGAGCTTCGAGAACTTTCTCCCTGGGCTGCCCGCATC 240 Leu Gin Gly Ala Pro Asp Ala Val Glu Leu Ara Glu Leu Ser Pro Trp Ala Ala Ara Ile CCGGGACCGCCGTCGAGCGGGTCCCCGGCGTCGGCGGGGGCCGGGGGGCTCGGCCT 300 Pro Gly Pro Ang Ang Ang Ala Gly Pro Ang Ang Ang Ang Ala Ang Pro Gly Ala Ang Pro TGTGGGCTGCGCGAGCTCGAGGTGCGCGTGAGCGAGCTGGGCCTGGGCTACACGTCGGAT 360 Cys Gly Leu Arg Glu Leu Glu Val Arg Val Ser Glu Leu Gly Leu Gly Tyr Thr Ser Asp GAGACCGTGCTGTTCCGCTACTGCGCAGGCGCGTGCGAGGCGGCCATCCGCATCTACGAC 420 Glu Thr Val Leu Phe Arg Tyr Cys Ala Gly Ala Cys Glu Ala Ala Ile Arg Ile Tyr Asp Leu Gly Leu Arg Arg Leu Arg Gln Arg Arg Arg Val Arg Arg Glu Arg Ala Arg Ala His Pro Cys Cys Arg Pro Thr Ala Tyr Glu Asp Glu Val Ser Phe Leu Asp Val His Ser Arg Tyr His Thr Leu Gln Glu Leu Ser Ala Arg Glu Cys Ala Cys Val 🔸

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Inventor(s):

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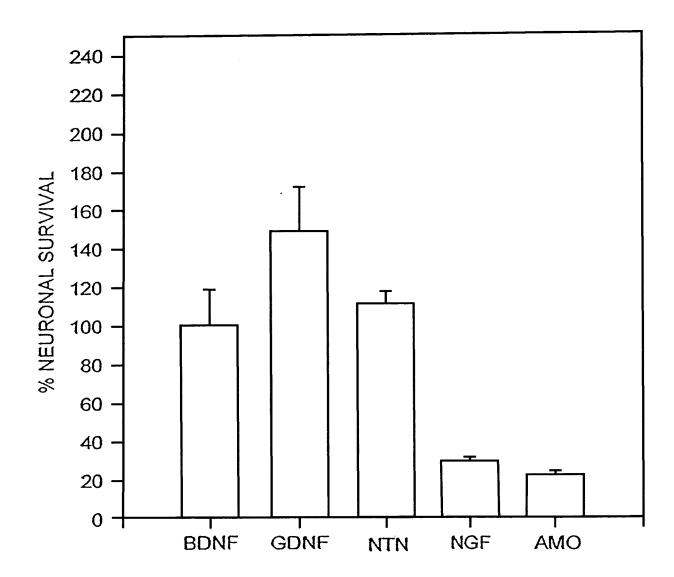


Figure 10

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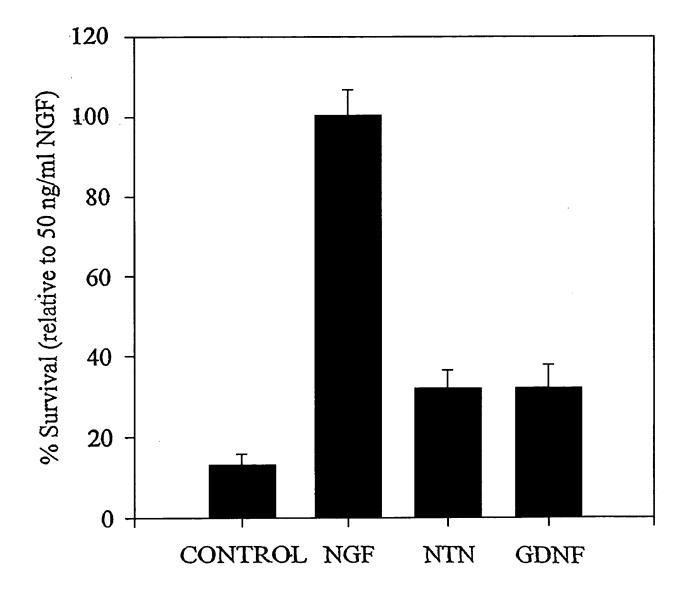


Figure 11

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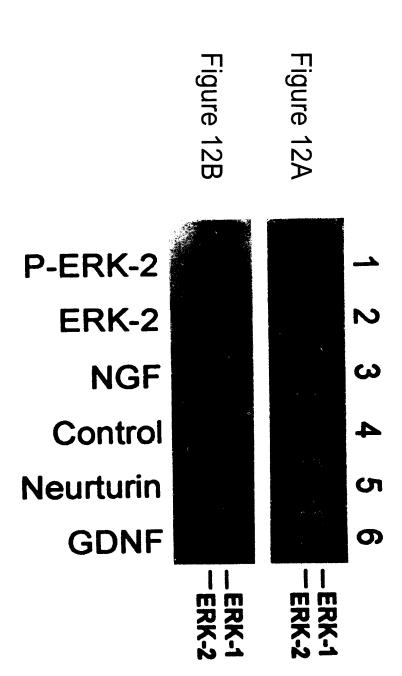
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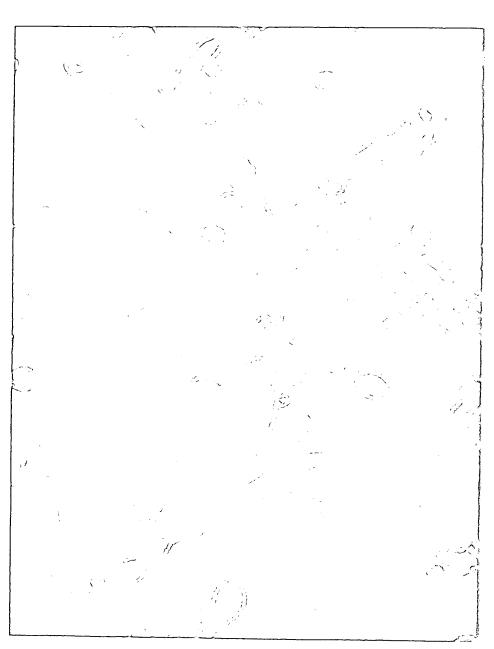


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Figure 13B. Neurturin-treated



Title:

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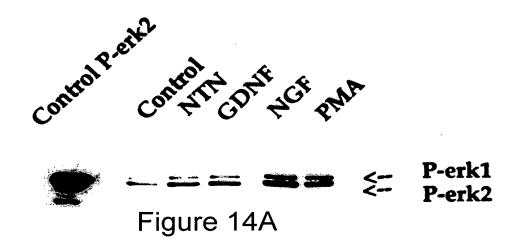
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## MAPK Response in Neuroblastoma Cell Lines

Figure 14A

SK-NSH Neuroblastoma (naive)



NGP Neuroblastoma (RA tx) Figure 14B

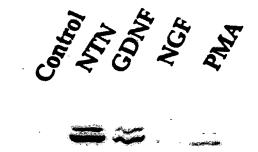


Figure 14C SY5Y Neuroblastoma (RX tx)





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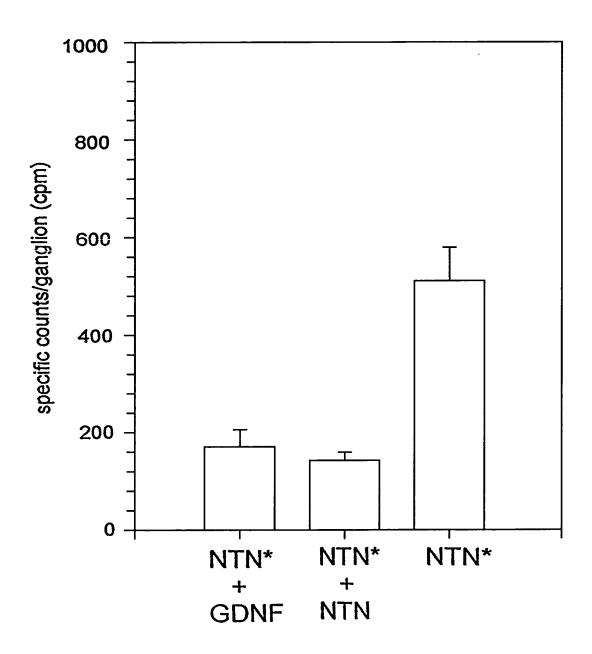


Figure 15

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CCURPLYIDEREDLIGWE. WIHEREGYNANFCAGACPYLWSSDTQHSRVLSLYNTINFEASAS-PCCVPQALEPLFIVYYGREFEVEQLSNWIVESCECS CCURPLYIDEREDLIGWE. WIHEREGYNANFCAGACPYLWSSDTQHSRVLSLYNTINFEASAS-PCCVSQDLEPLTILYYIGKTFEI	TGFS1 TGFS2 TGFS3 INHSA INHSA INHSB NODAL BMP2 BMP4 DPP BMP5 BMP6 BMP6 BMP6 BMP7 BMP7 BMP7 BMP7 BMP7 BMP7 BMP7 BMP7	11111111111111111111111111111111111111	Neurturin and Related Growth Fac Johnson et al. 09/476,290 - <u>Replacement Sheet</u> 56029-2669 17 / 19
SEQUENCE	GROWTH FACTOR	SEQ ID	tors

Figure 16

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108	106	104	102	101	100	9 Y 9 Q	97	96	95	94	93	92	91	90	89	8 8	87	86	NO:
GDNF GDNF	SINHO	DORSLN	GDF3	TOT	BMP3	60A	BMP7	BMP6	BMP5	440	BMP4	BMP2	NODAL	INHEB	INHGA	TGF83	TGFS2	TGF\$1	GROWTH FACTOR
CELHUFSLEFS-QUANDANT VAFRS INFS I CAGUCFOAVSHAILGEFYRIVSDKV-GQA CVLTAIHLAVT-DLGLGYETKEELIFRYCSGSCD-AAETTYDKILKNLSRNRRLVSDKV-GQA CGLRELEVRVS-ELGLGYASDETVLFRYCAGACE-AAARVYDLGLRRLRQRRRLRRERVRAQF	CHRVALNISF-QELGWERWIVYPESKIKHYCHGGCGLHIFKNLSLEVFGAFFIEAQFIGHL CALRELSVDLRAERSVLIPETYQANNCQGACGWPQSDRNPRYGNHVVLLLKMQARGATLARPP	CRRTSLHVNFK-EIGWDSWIIAPKDYBAFECKGGCFFPLTDNVTPTKHAIVQTLVHLQNPKK-ASKA	CHRHQLFINFQ-DLGWHKWVIAPKGFMANYCHGECPFSWITYLNSSNYAFMQALMHMADP-K-VPKA	CKKRHLYVEFK-DVGWQNWVIAPQGYMANYCYGECPYPLTEILNG8NHAILQTLVHSIEPED-IPLP		COMOTLY IDFK-DLGWHDWI IAPEGYGAFYCSGECNFPLNAHMNATNHAI VQTLVHLLEPKK-VPKP	CKKHELYVSFR-DLGWQDWIIAPEGYAAYYCEGECGFBLNSYMAATNHATUGLVHIMKDNA-VPKA				CRRHSLYVDF8-DVGWNDWIVAPFGYQAFYCHGDCPFPLADHLNSTNHAIVQTLVNSVNS-S-1FKA		CRRVKFQVDFN-LIGWGSWIIYPKQYNAYRCEGECPNPVGEEFHFTNHAYIQSLLKRYQPHR-VPST		CCKKOFFVSFK-DIGWNDWIIAPSGYHANYCEGECPSHIAG-TSGSSLSFHSTVINHYRMRGHSPFANLKS	CCVRPLYIDFRODLGWK-WVHEPKGYYANFCSGPCPYLRSADTTHSTVLGLYNTLNPKASAS-F	CCLRPLYIDFKRDLGWK-WIHEPKGYNANFCAGACPYLWSSDTQHSRVLSLYNTINFEASAS-F	CCVRQLYIDFRKDLGWK-WIHEPKGYHANFCLGPCPYIWSLDTQYSKVLALYNQHNPGASAA-P	SEQUENCE

Neurturin and Related Growth Factors

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SEQ		
ID	GROWTH	
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113	INHBA	CCVPTKLRPMSMLYYDDGQNII-KKDIQNMIVEECGCS
114	INHBB	CCIPTKLSTMSMLYFDDEYNIV-KRDVPNMIVEECGCA
115	NODAL	CCAPVKTKPLSMLYVDNGRVLLEHHKDMIVEECGCL
116	BMP2	CCVPTELSAISMLYLDENEKVVLK-NYQDMVVEGCGCR
117	BMP4	CCVPTELSAISMLYLDEYDKVVLK-NYQEMVVEGCGCR
118	DPP	CCVPTQLDSVAMLYLNDQSTVVLK-NYQEMTVVGCGCR
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121	BMP7	CCAPTQLNAISVLYFDDSSNVILK-KYRNMVVRACGCH
122	BMP8	CCAPTKLSATSVLYYDSSNNVILR-KHRNMVVKACGCH
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125	VG1	CCVPTKMSPISMLFYDNNDNVVLR-HYENMAVDECGCR
126	GDF1	CCVPARLSPISVLFFDNSDNVVLR-QYEDMVVDECGCR
127	GDF3	VCVPTKLSPISMLYQDSDKNVILR-HYEDMVVDECGCG
128	DORSLN	CCVPTKLDAISILYKDDAGVPTLIYNYEGMKVAECGCR
129	INHa	CCAALPGTMRPLHVRTTSDGGYSFKYETVPNLLTQHCACI
130	MIS	CCVPTAYTGKLLISLSEERISAHHVPNMVATECGCR
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